

**Amendments to the Drawings:**

The three attached replacement sheets containing new corrected drawings replace Figures 6A, 6B, 6C and 6D filed on September 12, 2001 and April 19, 2004. The changes in new corrected Figures 6A, 6B and 6C over original Figure 6 as filed on June 12, 2001 are shown in the three annotated sheets, which introduces the SEQ ID Nos. directly in the figure.

Attachment: Three (3) Replacement Sheets containing Figures 6A, 6B and 6C.  
Three (3) Annotated Sheets Showing Changes in Figures 6A, 6B and 6C over original Figure 6 as filed.

## REMARKS

The Examiner has required new corrected drawings in a communication dated August 25, 2004. Specifically, the Examiner stated that:

the sequences depicted in Figures 6A-6D do not correspond to the description of Figure 6 in the specification. In particular, while the description of Figure 6 recites "(SEQ ID Nos: 6-25, 20, 21, 26-43, 65, 66, 44-63, 67, 64 respectively)," a review of the sequences of Figures 6A-6D (as compared to Applicant's Sequence Listing) reveals that this order does not in fact correspond to the order of the sequences depicted in proposed Figures 6A-6D.

Accordingly, in response Applicants submit new corrected Figures 6A, 6B and 6C, contained in the three Replacement Sheets of drawings, which replace the drawings submitted on September 12, 2001. Changes in the new corrected Figures 6A, 6B and 6C over original Figure 6 as filed on June 12, 2001 are shown in the three Annotated Sheets Showing Changes. The amendment over original Figure 6 as filed has been made merely to introduce the SEQ ID Nos. directly in the figure, which eliminates the confusion in the order of the sequences that was noted by the Examiner.

Since the SEQ ID Nos. are now directly contained in Figures 6A-6C, Applicants have amended the specification to delete the references to SEQ ID Nos. in the figure caption and to update reference to Figures 6A-6C. No new matter has been added with this amendment. Applicants also submit a Sequence Listing which reflects the SEQ ID Nos. in the new corrected drawings, in compliance with 37 C.F.R. §§ 1.821 through 1.825.

Applicants respectfully request that the amendments and remarks made herein be entered and made of record in the file history of the instant application.

Respectfully submitted,

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Enclosure

1. 'A' Allele, CYP2D6\*3, A21337 deletion, Frameshift resulting in zero enzyme activity  
2637

added

2. 'B' Allele, CYP2D6\*4, G1934A, Spliceing defect resulting in zero enzyme activity

A. wt Probe - CYPwt (-) B1922 (C/A to mut at base 5) & CYPmut (+) B1922 (A/C to mut at base 13)

added

B. CYPwt (-)B1930 (C/A to mut at base 13) and CYPmut (+)B1930 (A/C to wt at base 5)

SSEQ	ID NO:22	NH2	3'- GGGTCTCGGGGAAAG -5'		CYPwt (-)	B1930,	17mer,	71%GC,	Tm=56C
SSEQ	ID NO:23	NH2	3'- (A)30GGGTCTCGGGGAAAG -5'		CYPwt (-)	B1930(A)	30-3'	NH2	
SSEQ	ID NO:24		5'- CCCAAGACGCCCTTTTC -3' NH2		CYPMut (+)	B1930,	17mer,	65%GC,	Tm=54C
SSEQ	ID NO:25		5'- CCCAAGACGCCCTTTTC (A)30 -3' NH2	-1909	CYPMut (+)	B1930 (A)	30-3'	NH2	
SSEQ	ID NO:26		5'- CCCTTACC GCATCTCCACCCCCAGGACGCCCTTTTCGCCCAACGGTGCT -3'		wild Type (+)				
SSEQ	ID NO:27		5'- CCCTTACC GCATCTCCACCCCCAAGACGCCCTTTTCGCCCAACGGTGCT -3'		Mut (+)				

FIGURE 6B

3. 'C' Allele, CYP2D6\*9, G2702-A2704 deletion, decreased enzyme activity

SEQ ID NO:28	5'- GCAGAGATGGAGAAGGTGAGAG -3' NH2	CYPwt (+) C2691, 22mer, 55%GC, Tm=60C
SEQ ID NO:29	5'- GCAGAGATGGAGAAGGTGAGAG (A) 30 -3' NH2	CYPwt (+) C2691 (A) 30-3' NH2
SEQ ID NO:30	5'- CAGAGATGGAGAAGGTGAGAG (A) 30 -3' NH2	CYPwt (+) C2692 (A) 30-3' NH2
SEQ ID NO:31	5'- GCAGAGATGGA---GGTGAGAGTG -3' NH2	CYPmut (+) C2691, 21mer, 57%GC, Tm=60C
SEQ ID NO:32	5'- GCAGAGATGGA---GGTGAGAGTG (A) 30 -3' NH2	CYPmut (+) C2691 (A) 30-3' NH2
SEQ ID NO:33	5'- CAGAGATGGA---GGTGAGAGTG (A) 30 -3' NH2	CYPmut (+) C2692 (A) 30-3' NH2
SEQ ID NO:34	3'- TGACTCCGGAAGGACCGTCTCTACCTCTTCCACTCTCACCGACGGTGCCAC -5'	Wild Type (-)
SEQ ID NO:35	3'- TGACTCCGGAAGGACCGTCTCTACCT--CCACTCTCACCGACGGTGCCAC -5'	Mut (-)

4. 'E' Allele, CYP2D6\*7, A3023C, H324P amino acid change results in zero enzyme activity

A. wt Probe - CYPwt (-) E3009 (T/C to mut at base 5) & CYPmut (+) E3009 (C/A to wt at base 15)

SEQ ID NO:36	NH2 3'- CGAGTACTAGGATGTAGGC -5'	CYPwt (-) E3009, 19mer, 53%GC, Pred Tm=57
SEQ ID NO:37	NH2 3'- (A) 30CGAGTACTAGGATGTAGGC -5'	CYPwt (-) E3009 (A) 30-3' NH2
SEQ ID NO:38	5'- GCTCATGATCCTACCTCCG -3' NH2	CYPmut (+) E3009, 19mer, 58%GC, Pred Tm=59C
SEQ ID NO:39	5'- GCTCATGATCCTACCTCCG (A) 30 -3' NH2	CYPmut (+) E3009 (A) 30-3' NH2
SEQ ID NO:40	5'- TGGGGCCTCCTGCTCATGATCCTACATCCGGATGTGCAGC   GTGAGCCCATC -3'	Wild Type (+)
SEQ ID NO:41	5'- TGGGGCCTCCTGCTCATGATCCTACCTCCGGATGTGCAGC   GTGAGCCCATC -3'	Mut (+)

B. CYPwt (-) E3018 (T/C to mut at base 14) and CYPmut (+) E3018 (C/T to wt at base 6)

SEQ ID NO:42	NH2 3'- GGATGTAGGCCTACACGTC -5'	CYPwt (-) E3018, 19mer, 58%GC, Tm=60
SEQ ID NO:43	5'- CCTACATCCGGATGTGCAG -3'	CYPwt (+) E3018 - Target
SEQ ID NO:44	5'- CCTACCTCCGGATGTGCAG -3' NH2	CYPmut (+) E3018, 19mer, 63%GC, Tm=62C
SEQ ID NO:45	3'- GGATGGAGGCCTACACGTC -5'	CYPmut (-) E3018 - Target
SEQ ID NO:46	5'- TGGGGCCTCCTGCTCATGATCCTACATCCGGATGTGCAGC   GTGAGCCCATC -3'	Wild Type (+)
SEQ ID NO:47	5'- TGGGGCCTCCTGCTCATGATCCTACCTCCGGATGTGCAGC   GTGAGCCCATC -3'	Mut (+)

FIGURE 6C

5. 'G' Allele, CYP2D6\*8, G1846T, Stop codon, zero enzyme activity

1846  
5' - CACTCCGGTGGGTGATGG (A) 30 -3' NH2 CYPwt (+) G1840 (A) 30-3' NH2, 18mer, 67%GC, Tm=60  
NH2 3' - (A) 30GTGAGGC'CACTACTACC -5' CYPwt (-) G1840 (A) 30-3' NH2  
5' - CACTCTGTGGGTGATGG (A) 30 -3' NH2 CYPmut (+) G1840 (A) 30-3' NH2, 18mer, 61%GC, Tm=57  
5' - GTGCCCGCTTCGCCACTCC | GTGGGTGATGGCAGAGGGCACAAGCGGG -3'  
5' - GTGCCCGCTTCGCCACTCC | TGTGGGTGATGGCAGAGGGCACAAGCGGG -3'  
Exon 3 end - | -1846

6. 'T' Allele, CYP2D6\*6, T1795 deletion, Frameshift resulting in zero enzyme activity

5' - GCTGGAGCAGTGGGTGAC -3' NH2 CYPwt (+) T1785, 18mer, 67%GC, Trn=59-61C  
5' - GCTGGAGCAGTGGGTGAC (A) 30 -3' NH2 CYPwt (+) T1785 (A) 30-3' NH2  
5' - CTGGAGCAGTGGGTGAC (A) 30 -3' NH2 CYPwt (+) T1786 (A) 30-3' NH2  
5' - GCTGGAGCAG-GGGTGAC -3' NH2 CYPmut (+) T1785, 17mer, 71 %GC, Tm=58-60C  
5' - GCTGGAGCAG-GGGTGAC (A) 30 -3' NH2 CYPmut (+) T1785 (A) 30-3' NH2  
5' - CTGGAGCAG-GGGTGAC (A) 30 -3' NH2 CYPmut (+) T1786 (A) 30-3' NH2  
-1773  
5' - GGGCAAGAAGTCGCTGAGCAGTGGGTGACCGAGGAGCGCCCTGCCT -3' Wild Type (+)  
5' - GGGCAAGAAGTCGCTGAGCAG-GGGTGACCGAGGAGCGCCCTGCCT -3' Mut (+)

7. 2D6/2D7/2D8 Controls - The 2D6/7/8 probes were designed in the 1600 region of the 2D6 gene. The purpose of the designs was to find region somewhere between the PCR primers were it would be easy to discriminate between 2D6 and its two pseudogenes, 2D7 and 2D8. The purpose of the designs is to demonstrate that the PCR amplicon is from the 2D6 gene, not one of the pseudogenes.

5' - GACCAGGGGGAGC-ATAGG (A) 30-3' NH2 CYP2D6wt (+) 1607 (A) 30-3' NH2  
5' - GACCTTGTGGAGCGCCAG (A) 30-3' NH2 CYP2D7wt (+) 1607 (A) 30-3' NH2  
5' - GACCAGGAAAAGC-ACAGG (A) 30-3' NH2 CYP2D8wt (+) 1607 (A) 30-3' NH2  
5' - GACCAGGAAAAGC-ACAGG (A) 30-3' NH2 CYP2D8wt (+) 1607b (A) 30-3' NH2  
-1603  
5' - GGGAGACCCAGGGGAGC-ATAGGTTGGAGTGGTGGT -3' 2D6 (+)  
5' - GGGAGACCTTGTGGAGCGCCAGGTTGGAGTGGTGGC -3' 2D7 (+)  
5' - GGGAGACCCAGGAAAAGC-ACAGGTTGGAGTGGGCGGC -3' 2D8 (+)

8. Pos/Neg Control probes- These probes were designed as true positive and negative control probes. They consist of the same semi-random sequence, with the positive control probe having a 5' Biotin.

5' Biotin- ATCATTCCTCAATCATCATATCATC (A) 25 -3' NH2 CYP (+) ran (A) 25-5' Biotin, 3' NH2  
5' - ATCATTCCTCAATCATCATATCATC (A) 25 -3' NH2 CYP (+) ran (A) 25-3' NH2